UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,347	02/27/2006	Jost Seibler	100725-47 (KGB)	3093

27384 7590 08/06/2008

NORRIS, MCLAUGHLIN & MARCUS, PA
875 THIRD AVENUE
18TH FLOOR
NEW YORK, NY 10022

EXAMINER	
NOBLE, MARCIA STEPHENS	

ART UNIT	PAPER NUMBER
1632	

MAIL DATE	DELIVERY MODE
08/06/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,347	SEIBLER ET AL.	
	Examiner	Art Unit	
	MARCIA S. NOBLE	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *41-44* is/are pending in the application.

4a) Of the above claim(s) *14-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 April 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/14/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group V, claims 41-44, in the reply filed on 5/30/2008 is acknowledged. The traversal is on the ground(s) that Applicant reserves the right to present evidence at a later time proving that Paddison is not prior art and that group I is closely connected with group V and therefore should be examined together . This is not found persuasive because first stating that Paddison is not prior art does not demonstrate as such. Paddison discloses a method of transfecting mammalian cells with a plasmid encoding a short hairpin RNA operably linked to and ubiquitous promoter, therefore meeting the limitations of claim 1 and demonstrating a lack of a novel special technical feature. The invention of Group I is drawn to an in vitro method of gene knock down in vertebrate cells using a short hairpin RNA expression vector. While the invention of Group I is related to group V, it is an in vitro method and the outcome is transfected cells, not a transgenic mouse, as encompassed by group V. Therefore the groups are distinct and should be examined separately.

The requirement is still deemed proper and is therefore made FINAL.

Claims 14-40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 5/30-2008. Claims 41-44 are under consideration.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claim 41 rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 40 is drawn to "A vertebrate...having stably integrated...an expression vector". This encompasses a genetically modified human, which is considered non-statutory subject matter.

The claims encompass transgenic humans which is subject matter precluded by the PTO policy (1077 O.G. 24 April 21, 1987). This rejection can be overcome by inserting "nonhuman" before vertebrate.

Claim Rejections - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 41-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 41 and 42 recite, "derived" or "a derivative". The metes and bounds of these terms are indefinite because "derived" or "derivative" suggest that some form of a manipulation has occurred to result in whatever has been "derived". Therefore it is unclear how closely related or similar the "derivative" is to the unmodified entity from

which it has been "derived". A suggestion for applicant would be to amend the claim to delete "derived" and replace it with "isolated" or "obtained".

Also, the "preferably" term in claim 41 is confusing as applicant has broad and narrow limitations within the same the claim. A suggestion is for applicant to delete the "preferably" phrase from claim 41 and add a new claim limited to the subject matter contained therein.

Claim 43 depends from claim 41.

Claim Rejections - 35 USC § 112, 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 41-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a **mouse** having stably integrated an expression vector comprising a shRNA construct under control of a ubiquitous promoter at a polymerase II dependent locus of the mouse genome by homologous recombination, wherein expression of said shRNA results in repression of expression of a gene targeted by said shRNA in said mouse, does not reasonably provide enablement for 1) a vertebrate other than a mouse having stably integrated said expression vector into a polymerase II dependent locus, and 2) a transgenic vertebrate with no phenotype. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use/make the invention commensurate in scope with these claims.

When determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make or use the claimed invention, if not, whether an artisan would require undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirements, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is "undue".

1) The instant claims broadly embrace the production of any transgenic vertebrate with a targeted insertion of the transgene into a polymerase II dependent locus by homologous recombination. However, the specification only teaches the production of a mouse comprising a targeted insertion in its genome.

The specification discloses the production of mouse ES cells comprising the firefly luciferase gene inserted into the first allele of the rosa26 locus by homologous recombination. A shRNA expression cassette under the control of the H1 or H6 promoter and a Renilla luciferase gene were inserted into these mouse ES cells at the second allele of the rosa26 locus by homologous recombination (Example 1, p. 18, lines 1-6). The specification discloses that the shRNA expression cassette can also be under the control of U6 promoter containing a tet operator sequence to allow for inducible control of the shRNA expression cassette (Example 2, p. 18, par 3, lines 1-4). The

specification discloses that these recombinant mouse ES cell were injected into diploid blastocysts and ultimately produced transgenic mice expressing the shRNA expression vector.

At the time of filing and presently, the art teaches that gene-targeting in vivo required homologous recombination in cells in vitro. The only cells that can be cultured in vitro that are competent to populate the germline and thereby make an animal are mouse ES cells. Thus, ES cell use for the generation of targeted genetically modified animals, such as knockin or knockout animals, has only been established in mice. Denning and Priddle state, "...pluripotent embryonic stem (ES) cells, which have been central to success in mice, are not available in any domestic species, despite considerable efforts to isolate them." (Reproduction 126:1, col 2, par 1, 2003). Since the art does not teach a means of making targeted insertions by homologous recombination in other species than mice, an artisan would look to the specification for specific guidance from the specification. However, the specification only provides specific guidance for the mouse. Therefore, the specification fails to provide specific guidance to predictably teach a means of making a transgenic vertebrate with a targeted insertion of an expression vector in any other vertebrate than mouse without undue experimentation.

2) The claims encompass a transgenic vertebrate that lacks a phenotype. The specification teaches that the purpose of the instant invention is to provide knock down animal with the use of shRNA expression vectors (p. 1, lines 1-3). The specification teaches the expression of the shRNA transgene encoding firefly luciferase by the

transgenic mouse efficiently represses firefly luciferase activity in most organs (p. 19, Example 4, last par, lines 7-10). Therefore, the specification provides specific guidance to a transgenic mouse comprising a phenotype. However, the specification fails to provide specific guidance to teach the use of a transgenic vertebrate with no phenotype as claimed. Therefore, the specification does not provide an enabled use for a transgenic vertebrate with no phenotype.

Overall, the instant claims are not enabled for the full breadth of the claims because the art at the time of the invention teaches that, with the exclusion of mice, the production of transgenic vertebrates with a targeted insertion of an expression vector is not predictable. The instant claims are also not enabled for the full breadth of the claims which would encompass a transgenic vertebrate with no phenotype because the specification fails to provide an enabled use for such a transgenic vertebrate with no phenotype. Furthermore, the specification fails provide specific guidance to overcome these unpredictabilities in the art. Therefore, the instant claims are only enable for a mouse having stably integrated an expression vector comprising a shRNA construct under control of a ubiquitous promoter at a polymerase II dependent locus of the mouse genome by homologous recombination, wherein expression of said shRNA results in repression of expression of a gene targeted by said shRNA in said mouse.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claim 44 is rejected under 35 U.S.C. 102(b) as being anticipated by Paddison (Genes & Dev 16:948-958, April 2002; of record).

Paddison discloses an expression vector comprising the ubiquitous H6 promoter and nucleic acid encoding a shRNA to p53 (p. 957, col 1, par 2, lines 1-15). Therefore, Paddison anticipates claim 44.

7. Claims 41-43 are rejected under 35 U.S.C. 102(b) as being anticipated by McCaffrey et al. (Nature, 2002 Vol. 418, 38-39).

McCaffrey discloses a mouse expressing a functional shRNA expression vector from DNA template using RNA polymerase III promoters in inducing luciferase gene suppression (p. 38, col 1, par 1, line 5 to col 2, line 1; Figure 1 C-D and p. 39, col 1, 1st full par, lines 1-24). McCaffrey does not specifically disclose that the mouse has "stably integrated" the expression vector. However, because the claims do not specify into what the expression vector is "stably integrated", "stably integrated" can encompass integrated into a cell. McCaffrey discloses that the shRNA expression vector was delivered to liver cells using hydrodynamic transfection (p. 38, col 3, lines 1-7). Therefore, inherently McCaffrey discloses, "stably integrated", because the cells of the

mouse liver were transfected with the shRNA vector and the vector was expressed. McCaffrey does not disclose the limitation of "preferably at a polymerase II dependent locus". However, because this limitation recites "preferably", the claims do not require the limitation. Therefore, McCaffrey, discloses all the limitations of the claims 41-43.

This rejection can be over come by stating the expression vector is stably integrated into the genome of the mouse.

8. Claims 41-43 are rejected under 35 U.S.C. 102(e) as being anticipated by Beach (US patent Publication no. 2003/0084471, publication date 5/1/2003; filing date 1/22/2002).

Beach et al demonstrates that short hairpins encoded on a plasmid are effective in suppressing luciferase gene expression (Figure 42 and p. 7, par [0093], lines 1-7) in vivo. DNA oligonucleotides encoding 29 nucleotide hairpins corresponding to firefly luciferase were inserted into a vector containing the U6 promoter. Beach further disclose that one of skill can choose from amongst a range of vectors to either transiently or stably express an short hairpin. Beach et al also disclose non-limiting examples of vectors and strategies to stably express short dsRNAs using U6 and H1 promoters (p. 23, par [0251], line 1 to par [0253], line 8; Figures. 43-45). Beach et al teach and claim a non-human transgenic mammal having germline and/or somatic cells comprising a transgene encoding a dsRNA construct (p. 26, claim 28 and p. 2 par [0052], lines 1-12) that includes mouse (p. 12, par [0154], line 2). Beach et al demonstrates that a short hairpin is highly effective in specifically suppressing gene

expression of firefly or Renilla luciferase (Example 6, p. 22, par [0246], line 1 to p. 23, par [0250], line 8). Beach does not disclose the limitation of "preferably at a polymerase II dependent locus". However, because this limitation recites "preferably", the claims do not require the limitation.

Accordingly, Beach et al anticipate claims 41-43.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 41-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beach et al. (US patent Publication no. 2003/0084471, dated 5/1/2003, effective filing date 1/22/2002); Bronson et al (Proc Natl Acad Sci U S A 1996; 93:9067–9072) and Soriano et al (US patent 6,461,864, October 8, 2002).

Beach et al demonstrates that short hairpins encoded on a plasmid are effective in suppressing luciferase gene expression (Figure 42 and p. 7, par [0093], lines 1-7) in

vivo. DNA oligonucleotides encoding 29 nucleotide hairpins corresponding to firefly luciferase were inserted into a vector containing the U6 promoter. Beach further disclose that one of skill can choose from amongst a range of vectors to either transiently or stably express an short hairpin. Beach et al also disclose non-limiting examples of vectors and strategies to stably express short dsRNAs using U6 and H1 promoters (p. 23, par [0251], line 1 to par [0253], line 8; Figures. 43-45). Beach et al teach and claim a non-human transgenic mammal having germline and/or somatic cells comprising a transgene encoding a dsRNA construct (p. 26, claim 28 and p. 2 par [0052], lines 1-12) that includes mouse (p. 12, par [0154], line 2). Beach et al demonstrates that a short hairpin is highly effective in specifically suppressing gene expression of firefly or Renilla luciferase (Example 6, p. 22, par [0246], line 1 to p. 23, par [0250], line 8). Beach does not disclose the limitation of "preferably at a polymerase II dependent locus". However, because this limitation recites "preferably", the claims do not require the limitation. Since, Beach taught a method for luciferase gene suppression using a construct under the control of a ubiquitous promoter, it is inherent that it would randomly integrate into polymerase II dependent locus in order to induce luciferase gene suppression. However, Beach et al do not explicitly teach how an expression vector integrates through homologous recombination at polymerase II dependent locus.

Prior to instant invention, Bronson describes transgenic mice made by pro nuclear injection of DNA as an effective method of achieving expression of exogenous DNA sequences for many purposes, including over expression, mutant analysis,

promoter analysis (p. 9067, col 1, par 1, lines 1-5). Bronson also describes problems associated with DNA incorporated into the mouse germ line using this method includes random integration and unpredictable copy numbers. It is noted that Bronson provided motivation of targeting a single copy of a transgenic sequence to a chosen location in the genome such as HPRT. He discloses many advantages of targeting at specific locus including the ability to control copy number, the ability to insert the transgene into regions of chromatin compatible with a desired developmental and tissue-specific expression. Bronson also taught homologous recombination in murine ES cells to generate mice having a single-copy of a transgene inserted at a chosen site in the genome (p. 2, figure 2 and p. 9068, col 2, par 3, lines 1-11).

Soriano et al teach methods and vector constructs for the production of genetically engineered non-human animals, which ubiquitously express a heterologous DNA segment in Rosa 26 locus, which is a polymerase II dependent locus of a vertebrate (abstract and claim 1). Therefore, Soriano teaches a polymerase II dependent locus as claimed. It is noted that Soriano describes targeting region as a portion of a targeting construct which becomes integrated into an endogenous chromosomal location following homologous recombination between a homology clamp and an endogenous gene locus, such as a ROSA26, ROSA5, ROSA23, ROSA11, G3BP (BT5), or EphA2 gene locus sequence (column 3, lines 51-54). Soriano also discloses a schematic of G2BP gene showing the retroviral promoter trap insertion site and a cassette comprising the ROSAbgeo retroviral insert. Thus, Soriano taught a method of targeting region that is flanked on each side by a homology clamp, such that

a double-crossover recombination between each of the homology clamps and their corresponding endogenous gene sequences result in replacement of the portion of the endogenous gene locus by the targeting region.

It would have been obvious for one of ordinary skill in the art at the time of invention to modify the method the construct disclosed by Beach to include the shRNA construct into a specific locus by homologous recombination in mouse ES cells to generate mice having a single-copy of a transgene inserted at a chosen site in the genome. Bronson provided motivation by emphasizing that the use of a chosen site for a single copy of a transgene avoids many of the problems associated with randomly inserted transgenes (p. 9072, col. 1, last par, lines 1-7). Furthermore, Soriano had already disclosed the methods and vector constructs for the production of non-human transgenic animals, which ubiquitously express a heterologous DNA segment in Rosa 26 locus. The skilled artisan would have been motivated to make transgenic nonhuman animal that comprises stably integrated expression vector comprising a shRNA into a specific locus such as ROSA26 or HPRT by homologous recombination as discussed by Bronson and Soriano, as it would have suppressed the expression of transgene for sustained period.

One who would practiced the invention would have had reasonable expectation of success because Beach et al had already described a method for gene knockdown in a mice by transiently as well as stably expressing shRNA construct and it would have only required routine experimentation that were disclosed by Bronson and Soriano before filing of this application. One of ordinary skill in the art would have been

motivated to combine the teaching of Beach, Bronson and Soriano because a method of gene knockdown in a mouse comprising a shRNA construct under control of a ubiquitous promoter into a polymerase II dependent locus, ROSA26/HPRT locus, would have provided stable and sustained inhibition of transgene.

Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 41-44 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 27 and 30 of

amendment filed 5/30/2008 in copending Application No. 10/685,837. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the copending claims encompass the same scope.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim 41 of the instant invention broadly encompasses a vertebrate having stably integrated, preferably at a polymerase II dependent locus of the vertebrate, an expression vector comprising a short hairpin RNA construct under the control of a ubiquitous promoter. Claim 42 specifies that the vertebrate is a non-human vertebrate and claim 43 specifies the vertebrate as a mouse or fish. Claim 27 of the copending application recites the same limitations as claim 41 except claim 27 more narrowly specifies a mouse, which encompasses the limitations of claims 41-43 of the instant claims. Claim 27 of the copending application also more narrowly specifies that stable integration is by homologous recombination and that the ubiquitous promoter be selected from the group consisting of polymerase I, II, and III dependent promoters.

Claim 44 of the instant application broadly encompasses an expression vector comprising a short hairpin RNA construct under control of a ubiquitous promoter. Claim 30 of the copending application encompasses the same limitations but also specifies that the expression construct comprise homologous sequences which integrate at a polymerase II dependent locus of the genome of the mouse. Claim 30 also specifies that the ubiquitous promoter be selected from the group consisting of polymerase I, II, and III dependent promoters. Claim 30 of the copending application more narrowly

encompasses a species of the instantly claimed expression vector of claim 44 of the instant application. Therefore, claim 30 encompasses the same limitations as instant claim 44.

Sequence Compliance

11. The nucleotide sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825.

37 CFR 1.821(d) states: "[w]here the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description of claims, even if the sequence is also embedded in the text or the description or claims of the patent application.

Table 1 on page 9 and Table 2 on pages 10-14 of the specification comprises sequences that lack sequence identifiers.

Appropriate correction is required.

The absence of proper sequence listing did not preclude the examination on the merits however, **for a complete response to this office action, applicant must submit the required material for sequence compliance.**

Information Disclosure Statement

12. The information disclosure statement filed 4/15/2005 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. The examiner was able to retrieve and consider the U.S. patents and WO documents listed, but copies of the non-patent literature documents could not be located. It is noted, applicant states the instant application is a national stage application of PCT/X and references listed on the 1449 were cited on the search report associated with the PCT (IDS, filed April 15, 2005, page 3). However, no references have been filed in the instant application.

13. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCIA S. NOBLE whose telephone number is (571)272-5545. The examiner can normally be reached on M-F 9 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Marcia S. Noble
1632

/Peter Paras, Jr./
Supervisory Patent Examiner, Art Unit 1632